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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/576,724	05/23/2000	Vladka Curin-Serbec	201196/50 (80242/US)	3140

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Michael L. Goldman
NIXON PEABODY LLP
Clinton Square
P O Box 31051
Rochester, NY 14603

EXAMINER	
WINKLER, ULRIKE	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/576,724	CURIN-SERBEC, VLADKA	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10,12-14,20,24-27,31 and 32* is/are pending in the application.

4a) Of the above claim(s) *10,24-27 and 31* is/are withdrawn from consideration.

5)☒ Claim(s) *6 and 14* is/are allowed.

6)☒ Claim(s) *1-3,5,12 , 13, 20 and 32* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The Amendment filed July 26, 2002 (Paper No. 16) in response to the Office Action of April 23, 2002 is acknowledged and has been entered. Claims 1-5, 12-14, 20 and 32 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112

The rejection of claims 1-5, 12, 13 and 20 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specifically disclosed monoclonal antibody produced by the hybridoma CNCM- I-2476, does not reasonably provide enablement for other antibodies that are able to bind the prion specific protein structure while not binding the normal cellular form of the prion protein **is maintained** for reasons of record.

Applicant's arguments have been fully considered but are not deemed persuasive. Applicant argues that the instant invention provides the critical "three dimensional structure" that is different from the prior art and it is therefore predictable that other antibodies which have the quality of binding the disease specific form of the prion protein while not binding the cellular form of the prion protein may be obtained. Applicant's arguments are that the references cited in the scope of enablement rejection are not limited to the 13 amino acid segments set out in SEQ ID NO 1 or 2 but comprise peptides of 17 amino acids. The specification on page 9, lines 1-10 indicate that the entire C-terminal portion may be used with the proviso that the 3 dimensional structure is retained, the specification does not provide a means of determining the requisite 3

dimensional structure. Based on the indication that the entire C-terminal domain can be used, this would indicate that peptides larger than 13 amino acids will retain the requisite 3-dimentional structure. Fishleigh et al. (U.S. Pat. No. 5,773,572) and O'Rourke (U.S. Pat. No. 6,261,790 B1) teach that the production of antibodies that meet the limitation of binding the disease specific form while not binding the cellular form of the prion protein in a sample is not a trivial undertaking and is not predictable. Fishleigh et al. and O'Rourke immunize animals with peptides that the ordinary artisan would predict to have the essential 3-dimentional structure of SEQ ID NO: 1 or 2, yet the antibodies produced do not meet the requirement of binding the disease specific form while not binding the cellular form. Applicants have only provided a single antibody made by the disclosed method that meets the requirement of binding the disease specific form while not binding the cellular form. Given the difficulty in the art in producing an antibody that may meet this particular binding requirement, it appears that undue experimentation would be required to practice the claimed inventions with a reasonable expectation of success. Therefore, applicant is enabled only for the single disclosed antibody made from the CNCM- I-2476 hybridoma.

Claim Rejections - 35 USC § 102

The rejection of claims 1, 3-5, 13 and 20 under 35 U.S.C. 102(e) as being anticipated by O'Rourke (U.S. Pat. No. 6,261,790 B1) **is withdrawn** in view of applicant's amendments to the claims adding the limitation " when both isoforms are present in a sample in native, non-denatured state".

The rejection of claims 1, 2, 4, 5, 12, 13 and 20 under 35 U.S.C. 102(b) as being anticipated by Prusiner et al. (U.S. Pat. No. 5,846,533) **is maintained** for reasons of record.

Applicant's argues that the reference does not utilize competitive binding assays or controls in the ELISA or Western Blot assays. Applicant is reminded that a patent is presumed valid for what it shows. Claim 1 of the patent indicates that the antibody is characterized by binding to the disease form of the prion PrPSc *in situ*, meaning in the natural or original position of place. In the specification column 38, lines 21 and 21 the reference indicates that monoclonal antibodies are part of the claimed scope. Therefore, the instant invention rejected as being anticipated by Prusiner et al.

New Rejection:

Claims 1, 2, 3, 10, 13, 20 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Korth et al. (Nature, 1997).

The instant invention is drawn to an antibody that is able to bind to the disease specific form of the prion protein while not binding to the cellular form in a sample in which both forms are present and they are not denatured.

The transitional term "having" in "does not create a presumption that the body of the claim is open" *Crystal Semiconductor Corp. v. TriTech Microelectronics Int 'l Inc.*, 246 F.3d 1336, 1348, 57 USPQ2d 1953, 1959 (Fed. Cir. 2001). The term "having" must be interpreted in light of the specification to determine whether open or closed claim language is intended. The specification indicates that present invention relates to a peptide sequence shown by the SEQ ID NO: 1 and 2 (see specification page 11, lines 12-22) additionally the peptides may contain one or

more amino acid substitutions or deletions with the proviso that the 3 dimensional structure is maintained. The specification therefore, does not limit the sequence to the 13 amino acid segment of SEQ ID NO: 1 or 2. "the antibody of the present invention shall be capable to differentiate between PrP^{Sc} and PrP^{C} by selectively binding the three dimensional conformation of the C- terminal part of $PrPS^{C}$" (see specification page 7, lines 8-10). From the disclosure it appears that the mere presence of the 13 amino acids found in SEQ ID NO 1 or 2 is sufficient to provide "conformation critical to achieve the 3 dimensional structure" and the claims are therefore not limited to just the peptide but can include larger fragments that comprise the critical 3-dimetional structure.

Korth et al. discloses the production of monoclonal antibodies by immunizing mice with a recombinant prion protein which comprises the C-terminal portion of the PrP^{Sc}. The 15B3 antibody is able to recognize the disease specific form of the prion protein while not recognizing the cellular form (see figure 1). The antibody is able to bind the epitope set out in SEQ ID NO:2 and the epitope of SEQ ID NO: 1 having at least one or more substitutions. Therefore, the instant invention is anticipated by Korth et al.

Claims 1, 2, 3, 5, 10, 12, 13, 20 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Korth et al. (EP 0 861 900 A1).

The instant invention is drawn to an antibody that is able to bind to the disease specifc form of the prion protein while not binding to the cellular form in a sample in which both forms are present and they are not denatured.

The transitional term "having" in "does not create a presumption that the body of the claim is open" *Crystal Semiconductor Corp. v. TriTech Microelectronics Int 'l Inc.*, 246 F.3d 1336, 1348, 57 USPQ2d 1953, 1959 (Fed. Cir. 2001). The term "having" must be interpreted in light of the specification to determine whether open or closed claim language is intended. The specification indicates that present invention relates to a peptide sequence shown by the SEQ ID NO: 1 and 2 (see specification page 11, lines 12-22) additionally the peptides may contain one or more amino acid substitutions or deletions with the proviso that the 3 dimensional structure is maintained. The specification therefore, does not limit the sequence to the 13 amino acid segment of SEQ ID NO: 1 or 2. "the antibody of the present invention shall be capable to differentiate between PrP^{Sc} and PrP^{C} by selectively binding the three dimensional conformation of the C- terminal part of $PrPS^{C}$" (see specification page 7, lines 8-10). From the disclosure it appears that the mere presence of the 13 amino acids found in SEQ ID NO 1 or 2 is sufficient to provide "conformation critical to achieve the 3 dimensional structure" and the claims are therefore not limited to just the peptide but can include larger fragments that comprise the critical 3-dimetional structure.

Korth et al. discloses the production of monoclonal antibodies by immunizing mice with a recombinant prion protein, which comprises the C-terminal portion of the PrP^{Sc}. The 15B3 antibody is able to recognize the disease specific form of the prion protein while ot recognizing the cellular form. The antibody is able to bind the epitope set out in SEQ ID NO:2 and the epitope of SEQ ID NO: 1 having at least one or more substitutions. Therefore, the instant invention is anticipated by Korth et al.

Claim Objections

Claim 4 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims as written do not add to the monoclonal antibodies already present in claim 1. Correction is required.

Allowable subject matter

Claims limited to the specific monoclonal antibody derived from the CNCM- I-2476 hybridoma cell line would be allowable.

Conclusion

Claims 6 and 14 would be allowable if rewritten in independent form.

Claims 1-3, 5, 12, 13, 20 and 32 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The official fax phone number for the organization where this application or proceeding is assigned is 703-872-9306; for informal communications please use 703-746-3162.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD.
PATENT EXAMINER

10/31/03